CENTER FOR DRUG EVALUATION AND RESEARCH

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FINAL PRINTED LABELING

ASTRA MERCK
Wayne, PA 19087, USA

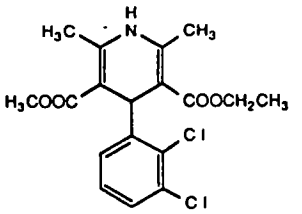
TABLETS

PLENDIL®

(FELODIPINE)
EXTENDED-RELEASE TABLETS

DESCRIPTION

PLENDIL* (Felodipine) is a calcium antagonist (calcium channel blocker). Felodipine is a dihydropyridine derivative that is chemically described as ± ethyl methyl 4-(2,3-dichlorophenyl)-1,4-dihydro-2,6-dimethyl-3,5-pyridinedicarboxylate. Its empirical formula is $C_{18}H_{19}Cl_2NO_4$ and its structural formula is:



Felodipine is a slightly yellowish, crystalline powder with a molecular weight of 384.26. It is insoluble in water and is freely soluble in dichloromethane and ethanol. Felodipine is a racemic mixture.

Tablets PLENDIL provide extended release of felodipine. They are available as tablets containing 2.5 mg, 5 mg or 10 mg of felodipine for oral administration. In addition to the active ingredient felodipine, the tablets contain the following inactive ingredients: Tablets PLENDIL 2.5 mg — hydroxypropyl cellulose, lactose, FD&C Blue 2, sodium stearyl fumarate, titanium dioxide, yellow iron oxide and other ingredients. Tablets PLENDIL 5 mg and 10 mg — cellulose, red and yellow oxide, lactose, polyethylene glycol, sodium stearyl fumarate, titanium dioxide and other ingredients.

CLINICAL PHARMACOLOGY

Mechanism of Action

Felodipine is a member of the dihydropyridine class of calcium channel antagonists (calcium channel blockers). It reversibly competes with nitrendipine and/or other calcium channel blockers for dihydropyridine binding sites, blocks voltage-dependent Ca^{++} currents in vascular smooth muscle and cultured rabbit atrial cells and blocks potassium-induced contracture of the rat portal vein.

In vitro studies show that the effects of felodipine on contractile processes are selective, with greater effects on vascular smooth muscle than cardiac muscle. Negative inotropic effects can be detected *in vitro*, but such effects have not been seen in intact animals.

The effect of felodipine on blood pressure is principally a consequence of a dose-related decrease of peripheral vascular resistance in man, with a modest reflex increase in heart rate (see *Cardiovascular Effects*). With the exception of a mild diuretic effect seen in several animal species and man, the effects of felodipine are accounted for by its effects on peripheral vascular resistance.

Pharmacokinetics and Metabolism

Following oral administration, felodipine is almost completely absorbed and undergoes extensive first-pass metabolism. The systemic bioavailability of PLENDIL is approximately 20 percent. Mean peak concentrations following the administration of PLENDIL are reached in 2.5 to 5 hours. Both peak plasma concentration and the area under the plasma concentration time curve (AUC) increase linearly with doses up to 20 mg. Felodipine is greater than 99 percent bound to plasma proteins.

Following intravenous administration, the plasma concentration of felodipine declined triexponentially with mean disposition half-lives of 4.8 minutes, 1.5 hours and 9.1 hours. The mean contributions of the three individual phases to the overall AUC were 15, 40 and 45 percent, respectively, in the order of increasing $t_{\frac{1}{2}}$.

Following oral administration of the immediate-release formulation, the plasma level of felodipine also declined polyexponentially with a mean terminal $t_{\frac{1}{2}}$ of 11 to 16 hours. The mean peak and trough steady-state plasma concentrations achieved after 10 mg of the immediate-release formulation given once a day to normal volunteers, were 20 and 0.5 nmol/L, respectively. The trough plasma concentration of felodipine in most individuals was substantially below the concentration needed to effect a half-maximal decline in blood pressure (EC_{50}) (4-6 nmol/L for felodipine), thus precluding once a day dosing with the immediate-release formulation.

Following administration of a 10-mg dose of PLENDIL, the extended-release formulation, to young, healthy volunteers, mean peak and trough steady-state plasma concentrations of felodipine were 7 and 2 nmol/L, respectively. Corresponding values in hypertensive patients (mean age 64) after a 20-mg dose of PLENDIL were 23 and 7 nmol/L. Since the EC_{50} for felodipine is 4 to 6 nmol/L, a 5 to 10-mg dose of PLENDIL in some patients, and a 20-mg dose in others, would be expected to provide an antihypertensive effect that persists for 24 hours (see *Cardiovascular Effects* below and DOSAGE AND ADMINISTRATION).

The systemic plasma clearance of felodipine in young healthy subjects is about 0.8 L/min and the apparent volume of distribution is about 10 L/kg.

Following an oral or intravenous dose of ^{14}C-labeled felodipine in man, about 70 percent of the dose of radioactivity was recovered in urine and 10 percent in the feces. A negligible amount of intact felodipine is recovered in the urine and feces (< 0.5%). Six metabolites, which account for 23 percent of the oral dose, have been identified; none has significant vasodilating activity.

Following administration of PLENDIL to hypertensive patients, mean peak plasma concentrations at steady state are about 20 percent higher than after a single dose. Blood pressure response is correlated with plasma concentrations of felodipine.

The bioavailability of PLENDIL is influenced by the presence of food. When administered either with a high fat or carbohydrate diet, C_{max} is increased by approximately 60 percent. AUC is unchanged. When PLENDIL was administered after a light meal (orange juice, toast and cereal), however, there is no effect on felodipine's pharmacokinetics. The bioavailability of felodipine was increased approximately two-fold when taken with grapefruit juice. Orange juice does not appear to modify the kinetics of PLENDIL. A similar finding has been seen with other dihydropyridine calcium antagonists, but to a lesser extent than that seen with felodipine.

Age Effects: Plasma concentrations of felodipine, after a single dose and at steady state, increase with age. Mean clearance of felodipine in elderly hypertensives (mean age 74) was only 45 percent of that of young volunteers (mean age 26). At steady state mean AUC for young patients was 39 percent of that for the elderly. Data for intermediate age ranges suggest that the AUCs fall between the extremes of the young and the elderly.

Hepatic Dysfunction: In patients with hepatic disease, the clearance of felodipine was reduced to about 60 percent of that seen in normal young volunteers.

Renal impairment does not alter the plasma concentration profile of felodipine; although higher concentrations of the metabolites are present in the plasma due to decreased urinary excretion, these are inactive.

Animal studies have demonstrated that felodipine crosses the blood-brain barrier and the placenta.

Cardiovascular Effects

Following administration of PLENDIL, a reduction in blood pressure generally occurs within two to five hours. During chronic administration, substantial blood pressure control lasts for 24 hours, with trough reductions in diastolic blood pressure approximately 40-50 percent of peak reductions. The antihypertensive effect is dose-dependent and correlates with the plasma concentration of felodipine.

A reflex increase in heart rate frequently occurs during the first week of therapy; this increase attenuates over time. Heart rate increases of 5-10 beats per minute may be seen during chronic dosing. The increase is inhibited by beta-blocking agents.

The P-R interval of the ECG is not affected by felodipine when administered alone or in combination with a beta-blocking agent. Felodipine alone or in combination with a beta-blocking agent has been shown, in clinical and electrophysiologic studies, to have no significant effect on cardiac conduction (P-R, P-Q and H-V intervals).

In clinical trials in hypertensive patients without clinical evidence of left ventricular dysfunction, no symptoms suggestive of a negative inotropic effect were noted; however none would be expected in this population (see PRECAUTIONS).

Renal/Endocrine Effects

Renal vascular resistance is decreased by felodipine while glomerular filtration rate remains unchanged. Mild diuresis, natriuresis and kaliuresis have been observed during the first week of therapy. No significant effects on serum electrolytes were observed during short- and long-term therapy.

In clinical trials in patients with hypertension increases in plasma noradrenaline levels have been observed.

Clinical Studies

Felodipine produces dose-related decreases in systolic and diastolic blood pressure as demonstrated in six placebo-controlled, dose response studies using either immediate-release or extended-release dosage forms. These studies enrolled over 800 patients on active treatment, at total daily doses ranging from 2.5 to 20 mg. In those studies felodipine was administered either as monotherapy or was added to beta

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blockers. The results of the two studies with PLENDIL given once daily as monotherapy are shown in the table below:

MEAN REDUCTIONS IN BLOOD PRESSURE (mmHg)*
Systolic/Diastolic

Dose	N	Mean Peak Response	Mean Trough Response	Trough/Peak Ratios (%s)
		Study 1 (8 weeks)		
2.5 mg	68	9.4/4.7	2.7/2.5	29/53
5 mg	69	9.5/6.3	2.4/3.7	25/59
10 mg	67	18.0/10.8	10.0/6.0	56/56
		Study 2 (4 weeks)		
10 mg	50	5.3/7.2	1.5/3.2	33/40**
20 mg	50	11.3/10.2	4.5/3.2	43/34**

*Placebo response subtracted
**Different number of patients available for peak and trough measurements

INDICATIONS AND USAGE

PLENDIL is indicated for the treatment of hypertension. PLENDIL may be used alone or concomitantly with other antihypertensive agents.

CONTRAINDICATIONS

PLENDIL is contraindicated in patients who are hypersensitive to this product.

PRECAUTIONS

General

Hypotension: Felodipine, like other calcium antagonists, may occasionally precipitate significant hypotension and rarely syncope. It may lead to reflex tachycardia which in susceptible individuals may precipitate angina pectoris. (See ADVERSE REACTIONS.)

Heart Failure: Although acute hemodynamic studies in a small number of patients with NYHA Class II or III heart failure treated with felodipine have not demonstrated negative inotropic effects, safety in patients with heart failure has not been established. Caution therefore should be exercised when using PLENDIL in patients with heart failure or compromised ventricular function, particularly in combination with a beta blocker.

Elderly Patients or Patients with Impaired Liver Function: Patients over 65 years of age or patients with impaired liver function may have elevated plasma concentrations of felodipine and may respond to lower doses of PLENDIL, therefore a starting dose of 2.5 mg once a day is recommended. These patients should have their blood pressure monitored closely during dosage adjustment of PLENDIL. (See CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION.)

Peripheral Edema: Peripheral edema, generally mild and not associated with generalized fluid retention, was the most common adverse event in the clinical trials. The incidence of peripheral edema was both dose- and age-dependent. Frequency of peripheral edema ranged from about 10 percent in patients under 50 years of age taking 5 mg daily to about 30 percent in those over 60 years of age taking 20 mg daily. This adverse effect generally occurs within 2-3 weeks of the initiation of treatment.

Information for Patients

Patients should be instructed to take PLENDIL whole and not to crush or chew the tablets. They should be told that mild gingival hyperplasia (gum swelling) has been reported. Good dental hygiene decreases its incidence and severity.

NOTE: As with many other drugs, certain advice to patients being treated with PLENDIL is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

Drug Interactions

Beta-Blocking Agents: A pharmacokinetic study of felodipine in conjunction with metoprolol demonstrated no significant effects on the pharmacokinetics of felodipine. The AUC and C_{max} of metoprolol, however, were increased approximately 31 and 38 percent, respectively. In controlled clinical trials, however, beta blockers including metoprolol were concurrently administered with felodipine and were well tolerated.

Cimetidine: In healthy subjects pharmacokinetic studies showed an approximately 50 percent increase in the area under the plasma concentration time curve (AUC) as well as the C_{max} of felodipine when given concomitantly with cimetidine. It is anticipated that a clinically significant interaction may occur in some hypertensive patients. Therefore, it is recommended that low doses of PLENDIL be used when given concomitantly with cimetidine.

Digoxin: When given concomitantly with PLENDIL the pharmacokinetics of digoxin in patients with heart failure were not significantly altered.

Anticonvulsants: In a pharmacokinetic study, maximum plasma concentrations of felodipine were considerably lower in epileptic patients on long-term anticonvulsant therapy (e.g., phenytoin, carbamazepine, or phenobarbital) than in healthy volunteers. In such patients, the mean area under the felodipine plasma concentration-time curve was also reduced to approximately six percent of that observed in healthy volunteers. Since a clinically significant interaction may be antici-

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pated, alternative antihypertensive therapy should be considered in these patients.

Other Concomitant Therapy: In healthy subjects there were no clinically significant interactions when felodipine was given concomitantly with indomethacin or spironolactone.

Interaction with Food: See CLINICAL PHARMACOLOGY, *Pharmacokinetics and Metabolism.*

Carcinogenesis, Mutagenesis, Impairment of Fertility

In a two-year carcinogenicity study in rats fed felodipine at doses of 7.7, 23.1 or 69.3 mg/kg/day (up to 28 times** the maximum recommended human dose on a mg/m² basis), a dose-related increase in the incidence of benign interstitial cell tumors of the testes (Leydig cell tumors) was observed in treated male rats. These tumors were not observed in a similar study in mice at doses up to 138.6 mg/kg/day (28 times** the maximum recommended human dose on a mg/m² basis). Felodipine, at the doses employed in the two-year rat study, has been shown to lower testicular testosterone and to produce a corresponding increase in serum luteinizing hormone in rats. The Leydig cell tumor development is possibly secondary to these hormonal effects which have not been observed in man.

In this same rat study a dose-related increase in the incidence of focal squamous cell hyperplasia compared to control was observed in the esophageal groove of male and female rats in all dose groups. No other drug-related esophageal or gastric pathology was observed in the rats or with chronic administration in mice and dogs. The latter species, like man, has no anatomical structure comparable to the esophageal groove.

Felodipine was not carcinogenic when fed to mice at doses up to 138.6 mg/kg/day (28 times** the maximum recommended human dose on a mg/m² basis) for periods of up to 80 weeks in males and 99 weeks in females.

Felodipine did not display any mutagenic activity *in vitro* in the Ames microbial mutagenicity test or in the mouse lymphoma forward mutation assay. No clastogenic potential was seen *in vivo* in the mouse micronucleus test at oral doses up to 2500 mg/kg (506 times** the maximum recommended human dose on a mg/m² basis) or *in vitro* in a human lymphocyte chromosome aberration assay.

A fertility study in which male and female rats were administered doses of 3.8, 9.6 or 26.9 mg/kg/day showed no significant effect of felodipine on reproductive performance.

Pregnancy

Pregnancy Category C

Teratogenic Effects: Studies in pregnant rabbits administered doses of 0.46, 1.2, 2.3 and 4.6 mg/kg/day (from 0.4 to 4 times** the maximum recommended human dose on a mg/m² basis) showed digital anomalies consisting of reduction in size and degree of ossification of the terminal phalanges in the fetuses. The frequency and severity of the changes appeared dose-related and were noted even at the lowest dose. These changes have been shown to occur with other members of the dihydropyridine class and are possibly a result of compromised uterine blood flow. Similar fetal anomalies were not observed in rats given felodipine.

In a teratology study in cynomolgus monkeys no reduction in the size of the terminal phalanges was observed but an abnormal position of the distal phalanges was noted in about 40 percent of the fetuses.

Nonteratogenic Effects: A prolongation of parturition with difficult labor and an increased frequency of fetal and early postnatal deaths were observed in rats administered doses of 9.6 mg/kg/day (4 times** the maximum human dose on a mg/m² basis) and above.

Significant enlargement of the mammary glands in excess of the normal enlargement for pregnant rabbits was found with doses greater than or equal to 1.2 mg/kg/day (equal to the maximum human dose on a mg/m² basis). This effect occurred only in pregnant rabbits and regressed during lactation. Similar changes in the mammary glands were not observed in rats or monkeys.

There are no adequate and well-controlled studies in pregnant women. If felodipine is used during pregnancy, or if the patient becomes pregnant while taking this drug, she should be apprised of the potential hazard to the fetus, possible digital anomalies of the infant, and the potential effects of felodipine on labor and delivery, and on the mammary glands of pregnant females.

Nursing Mothers

It is not known whether this drug is secreted in human milk and because of the potential for serious adverse reactions from felodipine in the infant, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

In controlled studies in the United States and overseas approximately 3000 patients were treated with felodipine as either the extended-release or the immediate-release formulation.

The most common clinical adverse events reported with PLENDIL administered as monotherapy at the recommended dosage range of 2.5 mg to 10 mg once a day were peripheral edema and headache. Peripheral edema was generally mild, but it was age- and dose-related and resulted in discontinuation of therapy in about 3 percent of the enrolled patients. Discontinuation of therapy due to any clinical adverse event occurred in about 6 percent of the patients receiving PLENDIL, principally for peripheral edema, headache, or flushing.

Adverse events that occurred with an incidence of 1.5 percent or greater at any of the recommended doses of 2.5 mg to 10 mg once a day (PLENDIL, N = 861; Placebo, N = 334), without regard to causality, are compared to placebo and are listed by dose in the table below. These events are reported from controlled clinical trials with patients who were randomized to a fixed dose of PLENDIL or titrated from an initial dose of 2.5 mg or 5 mg once a day. A dose of 20 mg once a day has been evaluated in some clinical studies. Although the antihypertensive effect of PLENDIL is increased at 20 mg once a day, there is a disproportionate increase in adverse events, especially those associated with vasodilatory effects (see DOSAGE AND ADMINISTRATION).

Percent of Patients with Adverse Events in Controlled Trials* of PLENDIL (N = 861) as Monotherapy without Regard to Causality (Incidence of discontinuations shown in parentheses)

Body System Adverse Events	Placebo N = 334	2.5 mg N = 255	5 mg N = 581	10 mg N = 408
Body as a Whole				
Peripheral Edema	3.3 (0.0)	2.0 (0.0)	8.8 (2.2)	17.4 (2.5)
Asthenia	3.3 (0.0)	3.9 (0.0)	3.3 (0.0)	2.2 (0.0)
Warm Sensation	0.0 (0.0)	0.0 (0.0)	0.9 (0.2)	1.5 (0.0)
Cardiovascular				
Palpitation	2.4 (0.0)	0.4 (0.0)	1.4 (0.3)	2.5 (0.5)
Digestive				
Nausea	1.5 (0.9)	1.2 (0.0)	1.7 (0.3)	1.0 (0.7)
Dyspepsia	1.2 (0.0)	3.9 (0.0)	0.7 (0.0)	0.5 (0.0)
Constipation	0.9 (0.0)	1.2 (0.0)	0.3 (0.0)	1.5 (0.2)
Nervous				
Headache	10.2 (0.9)	10.6 (0.4)	11.0 (1.7)	14.7 (2.0)
Dizziness	2.7 (0.3)	2.7 (0.0)	3.6 (0.5)	3.7 (0.5)
Paresthesia	1.5 (0.3)	1.6 (0.0)	1.2 (0.0)	1.2 (0.2)
Respiratory				
Upper Respiratory Infection	1.8 (0.0)	3.9 (0.0)	1.9 (0.0)	0.7 (0.0)
Cough	0.3 (0.0)	0.8 (0.0)	1.2 (0.0)	1.7 (0.0)
Rhinorrhea	0.0 (0.0)	1.6 (0.0)	0.2 (0.0)	0.2 (0.0)
Sneezing	0.0 (0.0)	1.6 (0.0)	0.0 (0.0)	0.0 (0.0)
Skin				
Rash	0.9 (0.0)	2.0 (0.0)	0.2 (0.0)	0.2 (0.0)
Flushing	0.9 (0.3)	3.9 (0.0)	5.3 (0.7)	6.9 (1.2)

*Patients in titration studies may have been exposed to more than one dose level of PLENDIL.

Adverse events that occurred in 0.5 up to 1.5 percent of patients who received PLENDIL in all controlled clinical trials at the recommended dosage range of 2.5 mg to 10 mg once a day and serious adverse events that occurred at a lower rate or events reported during marketing experience (those lower rate events are in italics) are listed below. These events are listed in order of decreasing severity within each category and the relationship of these events to administration of PLENDIL is uncertain: ***Body as a Whole:*** Chest pain, facial edema, flu-like illness; ***Cardiovascular:*** *Myocardial infarction, hypotension, syncope, angina pectoris, arrhythmia,* tachycardia, premature beats; ***Digestive:*** Abdominal pain, diarrhea, vomiting, dry mouth, flatulence, acid regurgitation; ***Hematologic:*** *Anemia;* ***Metabolic:*** ALT (SGPT) increased; ***Musculoskeletal:*** Arthralgia, back pain, leg pain, foot pain, muscle cramps, myalgia, arm pain, knee pain, hip pain; ***Nervous/Psychiatric:*** Insomnia, depression, anxiety disorders, irritability, nervousness, somnolence, decreased libido; ***Respiratory:*** Dyspnea, pharyngitis, bronchitis, influenza, sinusitis, epistaxis, respiratory infection; ***Skin:*** Contusion, erythema, urticaria; ***Special Senses:*** Visual disturbances; ***Urogenital:*** Impotence, urinary frequency, urinary urgency, dysuria, polyuria.

Gingival Hyperplasia: Gingival hyperplasia, usually mild, occurred in < 0.5 percent of patients in controlled studies. This condition may be avoided or may regress with improved dental hygiene. (See PRECAUTIONS, *Information for Patients.*)

Clinical Laboratory Test Findings

Serum Electrolytes: No significant effects on serum electrolytes were observed during short- and long-term therapy (see CLINICAL PHARMACOLOGY, *Renal/Endocrine Effects*).

Serum Glucose: No significant effects on fasting serum glucose were observed in patients treated with PLENDIL in the U.S. controlled study.

Liver Enzymes: One of two episodes of elevated serum transaminases decreased once drug was discontinued in clinical studies; no follow-up was available for the other patient.

OVERDOSAGE

Oral doses of 240 mg/kg and 264 mg/kg in male and female mice, respectively and 2390 mg/kg and 2250 mg/kg in male and female rats, respectively, caused significant lethality.

In a suicide attempt, one patient took 150 mg felodipine together with 15 tablets each of atenolol and spironolactone and 20 tablets of nitrazepam. The patient's blood pressure and heart rate were normal on admission to hospital; he subsequently recovered without significant sequelae.

Overdosage might be expected to cause excessive peripheral vasodilation with marked hypotension and possibly bradycardia.

**Based on patient weight of 50 kg

If severe hypotension occurs, symptomatic treatment should be instituted. The patient should be placed supine with the legs elevated. The administration of intravenous fluids may be useful to treat hypotension due to overdosage with calcium antagonists. In case of accompanying bradycardia, atropine (0.5-1 mg) should be administered intravenously. Sympathomimetic drugs may also be given if the physician feels they are warranted.

It has not been established whether felodipine can be removed from the circulation by hemodialysis.

DOSAGE AND ADMINISTRATION

The recommended starting dose is 5 mg once a day. Depending on the patient's response the dosage can be decreased to 2.5 mg or increased to 10 mg once a day. These adjustments should occur generally at intervals of not less than two weeks. The recommended dosage range is 2.5-10 mg once daily. In clinical trials, doses above 10 mg daily showed an increased blood pressure response but a large increase in the rate of peripheral edema and other vasodilatory adverse events (see ADVERSE REACTIONS). Modification of the recommended dosage is usually not required in patients with renal impairment.

PLENDIL should regularly be taken either without food or with a light meal (see CLINICAL PHARMACOLOGY, *Pharmacokinetics and Metabolism).* PLENDIL should be swallowed whole and not crushed or chewed.

Use in the Elderly or Patients with Impaired Liver Function: Patients over 65 years of age or patients with impaired liver function, may develop higher plasma concentrations of felodipine, therefore a starting dose of 2.5 mg once a day is recommended. Dosage may be adjusted as described above. (See PRECAUTIONS.)

HOW SUPPLIED

No. 3584 — Tablets PLENDIL, 2.5 mg, are sage green, round convex tablets, with code 450 on one side and PLENDIL on the other. They are supplied as follows:

NDC 61113-450-28 unit dose packages of 100
NDC 61113-450-58 unit of use bottles of 100
NDC 61113-450-31 unit of use bottles of 30.

No. 3585 — Tablets PLENDIL, 5 mg, are light red-brown, round convex tablets, with code 451 on one side and PLENDIL on the other. They are supplied as follows:

NDC 61113-451-28 unit dose packages of 100
(6505-01-350-0354, 5 mg individually sealed 100's)
NDC 61113-451-58 unit of use bottles of 100
(6505-01-350-0356, 5 mg 100's)
NDC 61113-451-31 unit of use bottles of 30
(6505-01-350-0352, 5 mg 30's).

No. 3586 — Tablets PLENDIL, 10 mg, are red-brown, round convex tablets, with code 452 on one side and PLENDIL on the other. They are supplied as follows:

NDC 61113-452-28 unit dose packages of 100
(6505-01-350-0353, 10 mg individually sealed 100's)
NDC 61113-452-58 unit of use bottles of 100
(6505-01-350-0355, 10 mg 100's)
NDC 61113-452-31 unit of use bottles of 30
(6505-01-350-0357, 10 mg 30's).

Storage

Store below 30°C (86°F). Keep container tightly closed. Protect from light.

Distributed by:

ASTRA MERCK

Wayne, PA 19087, USA

Manufactured by: MERCK & CO., Inc., West Point, PA 19486, USA

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